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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/659,698

09/11/2003

Richard M. Carlton

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11/28/2006

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EXAMINER

SNYDER, STUART

ART UNIT

PAPER NUMBER

1648

DATE MAILED: 11/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/659,698

Applicant(s)

CARLTON ET AL.

Examiner

Stuart W. Snyder

Art Unit

1648

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 September 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 15-17, 19 and 23-25 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 15-17, 19 and 23-25 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/5/2006 has been entered.

Status of the Claims

Claims 15-17, 19, 23-25 are subject to examination.

In view of Applicant's Declaration filed 9/5/2006 under 37 CFR 1.132, the previous rejection under 35 USC 103(a) is withdrawn.

Claim Rejections - 35 USC § 112, 1st Paragraph—Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

In view of Applicant's Declaration under 37 CFR 1.132 filed 9/5/2006, Claims 15-17, 19, and 23-25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Enablement is considered in view of the Wands factors (MPEP 2164.01(a)).

1. Nature of the invention and breadth of claims: The claims are drawn to PEGylated bacteriophage this is able to delay inactivation by an animal's host defense system (amended claim 17), has a 15% longer half-life than corresponding wild-type phage (amended claim 15), is specific for certain bacterial families (claim 16) and a method of making (claim 19) said phage, and pharmaceutical compositions thereof (claims 23-25).
2. State of the prior art: Applicant and the Office agree that the prior art taught PEGylation of pharmacologically important proteins but not bacteriophage.
3. Working examples: None. In a declaration by one of the inventors (CR Merrill), the following is admitted and/or alleged and is relevant to the instant rejection:
 - a. Dr. Merrill alleges in points 4-7 that there is a post-filing embodiment of the claimed invention and refers to scholarly articles authored by O'Riordan et al. in 1999. However, O'Riordan and others were experimenting with Adenoviruses that are not bacteriophages, the subject matter of applicants claimed invention
 - b. Dr. Merrill cites O'Riordan's and other groups use of Adenoviruses which do not have "tail" proteins, as specified in the method of production of applicants claimed invention, and therefore cannot be made by the method claimed by Applicants.
 - c. Dr. Merrill does not address the central issue posed in the instant application, PEGylation of the bacteriophage so that the modified bacteriophage "remain in the circulation and in the tissues longer than the

unmodified phage.” (page 1, lines 20 of the specification). Although the cited reference compares in vitro neutralization escape and in vivo transfection by PEGylated Adenovirus, there is no time-course comparison of Adenovirus numbers between PEGylated and non-PEGylated Adenoviruses in the mouse model.

4. Guidance in the specification: Applicants give the following guidance for PEGylating such bacteriophage (see p 9, lines 12-26):

“In the present invention, the adduct of the polymer with phage surface proteins is custom designed by methods known in the art, e.g. by: 1) varying the molecular weight of the polymer, 2) altering the reaction variables, for example: the concentrations of the reagents (such as the molecule used to activate the PEG reaction); the time course of the reaction (this changes the percentage of the amino acid groups of the phage surface antigen that become modified); the temperature; the pH; etc., 3) altering the type of PEG activator being used; and/or 4) altering the PEG derivative chosen for the reaction—one example among many being the bifunctional analog of SC-PEG known as poly(ethylene glycol)-bis-N-succinimidyl carbonate (“BSC-PEG”). These alterations provide a variety of physico-chemically altered bacteriophages, from which the ones demonstrating the best ability to delay inactivation by the HDS can be selected.”

Applicant additionally cites use of succinyl carbonate as a preferred method of activation of mPEG (see p 8, lines 25, 26); in a prophetic example of a method of making the claimed invention, Applicants again recite the use of succinyl carbonate for the activation of mPEG and

subsequent PEGylation by this activated form of PEG. Many of the other experimental variables of making the PEGylated bacteriophage are also specifically recited in the prophetic example.

5. Predictability of the art: Applicant admits that the art is unpredictable in the declaration filed Sep. 5, 2006; "The INOPERATIVE embodiments show unpredictability in the art even after the April 1994 filing date." (p 2, lines 3 and 4). In addition, O'Riordan et al. teaches that applicant's preferred method and the detailed prophetic example result in substantially inactivated virus in an adenovirus/mouse model which further suggests that Applicants' method would not be successful in delaying HDS inactivation of bacteriophage and that the art at the time of filing was unpredictable.
6. Amount of experimentation: Applicants admit that substantial experimentation was required to obtain satisfactory results in the adenovirus/murine model system: "The O'Riordan group explained in their discussion that various chemically activated forms of PEG were available when their work was begun [in 1999], but they would have to experiment to determine which form (if any) would be compatible with protection from antigenicity and retention of infectivity." (see p. 3, line 8 ff). Applicants' method further comprises protecting the "tail" proteins of bacteriophage with antibodies; this would entail antibody selection not only for "tail" protein specificity, but selection for antibodies that would not interfere with bacteriophage infectivity.

Art Unit: 1648

In summary, while the Office agrees with Applicant that one skilled in the art could attach PEG to a phage, there is no evidence that the PEGylated phage would possess the claimed property—i.e., delayed inactivation by the Host Defense System. This property is not shown in the specification or in the declaration with adenovirus. Given the breadth of the claims, the lack of guidance in the specification, and the unpredictability of the art as cited in the declaration, it would require undue experimentation for one skilled in the art to make and use the claimed composition as claimed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stuart W. Snyder whose telephone number is (571) 272-9945. The examiner can normally be reached on 9:00 AM-5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce R. Campell can be reached on (571) 272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



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